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United States Patent [19]

Gross**[11] Patent Number:** **5,880,124****[45] Date of Patent:** **Mar. 9, 1999****[54] BLOCKING INDUCTION OF TETRAHYDROBIOPTERIN TO BLOCK INDUCTION OF NITRIC OXIDE SYNTHESIS****[75] Inventor:** **Steven S. Gross**, New York, N.Y.**[73] Assignee:** **Cornell Research Foundation, Inc.**, Ithaca, N.Y.**[21] Appl. No.:** **642,883****[22] Filed:** **May 6, 1996****Related U.S. Application Data**

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[51] Int. Cl.⁶ **A61K 31/495; A61K 31/50****[52] U.S. Cl.** **514/253****[58] Field of Search** **514/253****[56] References Cited****U.S. PATENT DOCUMENTS**

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[57] ABSTRACT

Guanosine triphosphate pathway tetrahydrobiopterin synthesis antagonist and/or pterin salvage pathway tetrahydrobiopterin synthesis antagonists are administered to inhibit nitric oxide synthesis from arginine in vascular cells in a subject in need of such inhibition (e.g., for prophylactic or curative effect for endotoxin- or cytokine-induced hypotension or for restoration of vascular contractile sensitivity to pressor agents in the treatment of such hypotension). The tetrahydrobiopterin synthesis antagonist may be administered with α_1 -adrenergic agonist or with nitric oxide synthase inhibitor. The tetrahydrobiopterin synthesis antagonists are also administered to attenuate inflammation caused by induced nitric oxide production in immune cells. Unwanted counterproductive or side effects can be eliminated or ameliorated by administration additionally of levodopa with or without carbidopa and L-5-hydroxytryptophane.

15 Claims, 9 Drawing Sheets